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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,375	09/29/2005	Ragab El-Rashidy	GENIX-103	3124

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EXAMINER
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CORDERO GARCIA, MARCELA M

ART UNIT	PAPER NUMBER
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1654

MAIL DATE	DELIVERY MODE
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08/10/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/551,375	EL-RASHIDY, RAGAB	
	<b>Examiner</b>	<b>Art Unit</b>	
	Marcela M. Cordero Garcia	1654	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 May 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-24 and 26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-24 and 26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Applicant's election without traverse of the species "the method of treating advanced prostate cancer comprising administration of an injectable solution of leuprolide, calcitriol and polysorbitan" in the reply filed on May 16, 2007 is acknowledged.

Claims 1-24 and 26 are pending in the application.

Claims 1-24 and 26 are presented for examination on the merits.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4 and 16-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garnick et al. (US 5,780,435) in view of Beer et al. (Seminars in Oncology, August 2001) in further view of Lu et al. (US 5,284,657).

Garnick et al. teach administration of leuprolide in a sustained release formulation administered subcutaneously or intramuscularly (e.g., Examples 1-3) in order to treat advanced prostate cancer (e.g., claims 1-6, column 13, lines 24-26 and 45-56). The limitations "...injectable, sustained release depot formulation..." of claim 18 and "...single intramuscular injection per month of about 7.5 mg of leuprolide..." of claim

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20 are taught, e.g., at Example 2, lines 58-62. The limitation of claim 17 is taught, e.g., at "...about 1 milligram per day..." is taught, e.g., at column 15, line 24, which teaches 0.01 mg/kg, which reads upon a 1 mg dose for a subject with 100 kg. The limitations "...daily.." in claim 17 and "weekly.." in claim 19, "...three months..." in claim 21, "four months..." in claim 22 and "...one-year.." are not expressly taught, however, the disclosure of Garnick et al. teaches that "...a therapeutically effective amount refers to an amount effective, at dosages and for periods of time necessary to achieve the desired result." (e.g., column 15, lines 10-12). The limitations "...about 11.75 mg. In the form a three-month... formulation.", "...about 30 mg in the form of a four-month formulation" and "...about 65 mg in a form of a one-year implant" of claims 21, 22 and 23 are not expressly taught however, the disclosure of Garnick et al. teaches optimizing dosages for periods of time, depending on disease state, age and weight of the individual within 0.01 ug/kg-10mg/kg and preferably between about 0.01 to 5 mg/kg (e.g., column 15, lines 12-33). See also column 15, line 52, which teaches implants. The limitation "...isotonic.." of claim 17, is taught, e.g., at column 15, lines 34-36. The limitation "...saline..." of claim 17 is not expressly taught in Garnick et al.

Lu et al. is relied upon to teach the formula of leuprolide, which is 5-oxo-L-Pro-L-His-L-Trp-L-Ser-L-Tyr-D-Leu-L-Leu-L-Arg-Pro-N-ethylamide (e.g., column 3, lines 20-21, and Example 1) which reads upon the limitations of claims 2-4, wherein Xaa is D-Leu and Yaa is a modified proline residue (Pro-N-ethylamide, i.e., N-ethyl-L-prolinamide).

Garnick et al. and Lu et al. do not teach administering calcitriol with the leuprolide.

Beer et al. teach treating advanced prostate cancer (e.g., title of abstract) with a composition comprising calcitriol (lines 4-5). Beer et al. teach administering 0.5 ug/kg calcitriol orally (e.g., 60 kg patient: 30 ug).

It has been held that combinations of two or more compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is to be used for the very same purpose. In re Susi, 58 CCPA 1074, 1079-80, 440 F.2d 442, 445, 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21, 279 F.2d 274, 276-77, 126 USPQ 186, 188 (1960). As the court explained in Crockett, the idea of combining them flows logically from their having been individually taught in prior art. Therefore, since each of the reference teach that are effective in treating advanced prostate cancer, it would have been obvious to combine the two compounds with the expectation that such a combination would be effective in treating advanced prostate cancer. Thus, combining them flows logically from their having been individually taught in prior art. Please note that the combination above reads upon the limitation of claim 1: "... an amount of calcitriol sufficient to enhance the effectiveness of luteinizing hormone releasing hormone agonist analog against the advanced prostate cancer relative to treatment with luteinizing hormone releasing hormone agonist analog alone... ". The adjustment of particular conventional working conditions (e.g., determining appropriate dosages and periods of administration, making isotonic saline solutions, within such method of treating advanced prostate cancer as

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taught by Garnick et al., column 15) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan.

Claims 1, 5-15 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garnick et al. (US 5,780,435) in view of Beer et al. (Seminars in Oncology, August 2001) in view of Conway et al. (US 4,308,264) and in view of Chen (US 6,919,370).

Garnick et al. and Beer et al. are relied upon as above. Beer et al. teach the limitation of claims 14-15: "...about 0.1 to about 20 ug/kg based on the weight of the patient" (e.g., administering 0.5 ug/kg calcitriol, which is about 30 ug in a 60 kg patient claim 11: "about 5 to about 30 ug of calcitriol").

Garnick et al. and Beer et al. do not teach solutions comprising 1 to about 30 micrograms of calcitriol with a polysorbitan (a non-ionic surfactant) such as polysorbate 20.

Conway et al. teach isotonic solutions comprising a saline medium, polysorbate 20, ascorbic acid and calcitriol (e.g., column 4, lines 8-14). The limitation of claim 5: "...isotonic.." is taught at claim 15. The limitation "...and a sufficient quantity of nonionic surfactant to solubilize the calcitriol therein" is taught at "column 4, lines 19-21. The limitation of claim 8 "...about 1 to about 15 mg/mL of ascorbic acid" is taught at column 5, lines 5-15. The limitation of claim 10: "... about 1 to about 2 mg/mL of EDTA" is taught e.g., at lines 8-10 in column 5. The limitation of claim 13: "..about 1 to about 10

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mg/mL of polysorbitan" is taught e.g., at column 5, line 7. The limitation of claim 9:

"about 2 to about 6 mg/mL of ascorbic acid" is not expressly taught.

Chen teaches solutions comprising saline polysorbate 20 and leuprolide (e.g., column 7, lines 16-23; column 8, lines 35-38). It also teaches adding therein 'osteoporosis agents' (e.g., column 7, line 59), such as calcitriol. The limitation of claim 26 "about 5 to about 20 milligrams per milliliter of polysorbate 20" is taught, e.g., at formulation 5, column 19 of Chen and column 5, line 7 and claim 12 of Conway et al.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Garnick et al. and Beer et al. by making injectable isotonic saline solutions of calcitriol comprising polysorbitan 20, ascorbic acid and EDTA as taught by Conway et al. and Chen. The skilled artisan would have been motivated to do so because Conway et al. teach therapeutic injections of isotonic saline calcitriol (e.g., column 2, lines 64-67) solutions comprising the excipients claimed (polysorbitan 20, EDTA and ascorbic acid). There would have been a reasonable expectation of success, given that Chen teaches combinations of all the main components (leuprolide, an osteoporosis agent such as calcitriol and polysorbate 20) in saline media injections for anti-cancer treatment. Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made. The adjustment of particular conventional working conditions (e.g., determining appropriate dosages and formulations within such advanced prostate cancer treatment method) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. Thus the invention as a whole was

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clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

### ***Conclusion***

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcela M. Cordero Garcia whose telephone number is (571) 272-2939. The examiner can normally be reached on M-Th 7:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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